# A ferret that does not fare well

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**Signalment**:
1.5-year-old, male neutered ferret

**History and clinical findings:**
6-week history of diarrhea with intermittent melena, bruxism of increased frequency and severity, increasing lethargy and recent vomiting (twice). Treatment with Clavamox®, sucralfate, chloramphenicol, buprenorphine, and prednisolone had been ineffective. The ferret lives with another ferret. A cat is also present in the house but has no contact with the ferrets.

**Diagnostics**:
*Abdominal ultrasonography*
A well-marginated, irregularly-shaped, soft tissue mass in right cranial abdomen, enlarged mesenteric lymph nodes.

*Cytology*

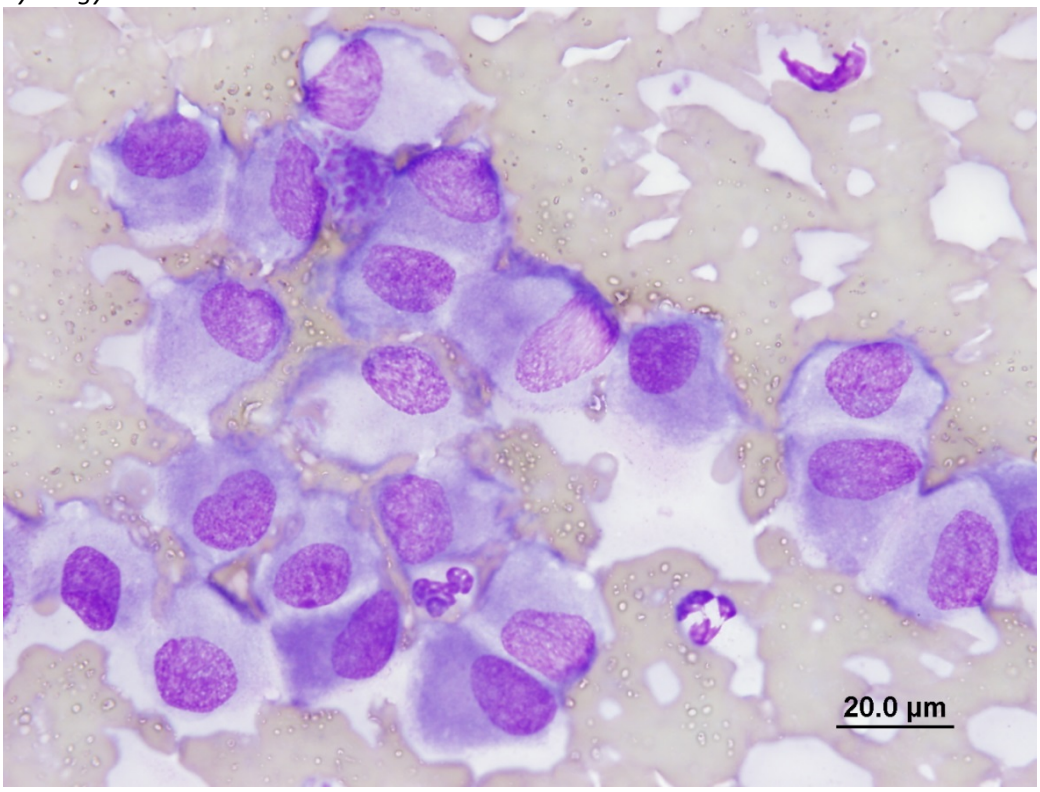


Figure 1
Fine needle aspirate of abdominal mass. Modified Romanowsky stain, 100x.

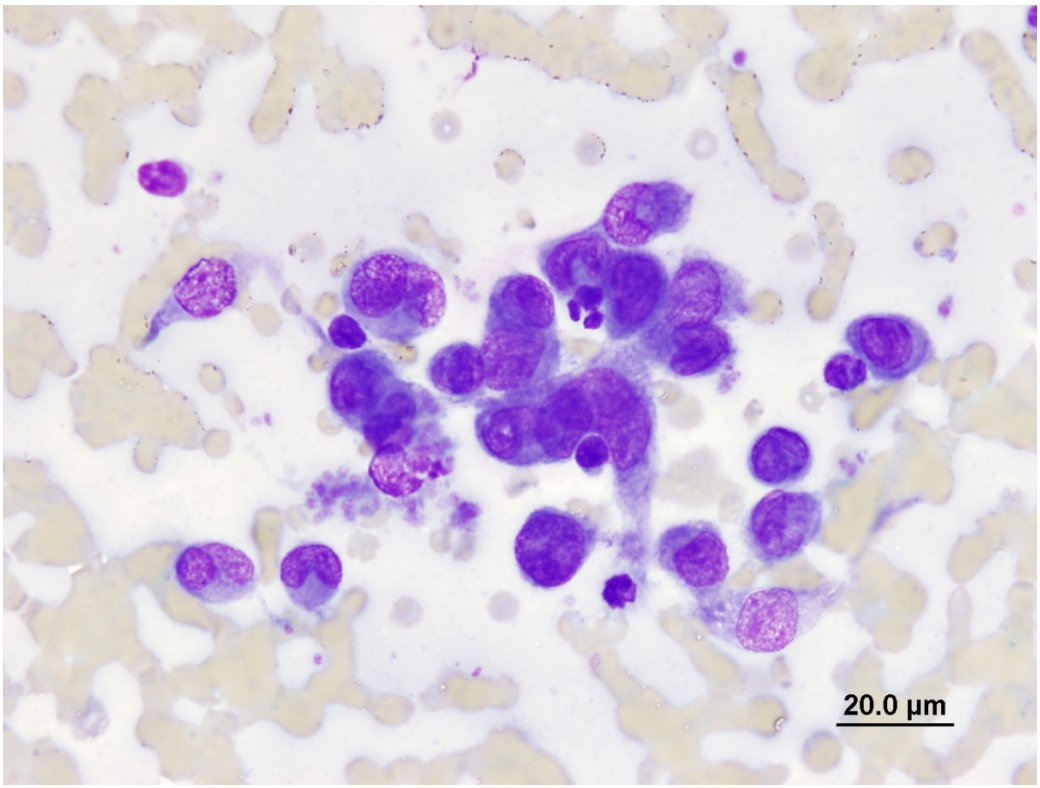


Figure 2
Fine needle aspirate of abdominal mass. Modified Romanowsky stain, 100x.

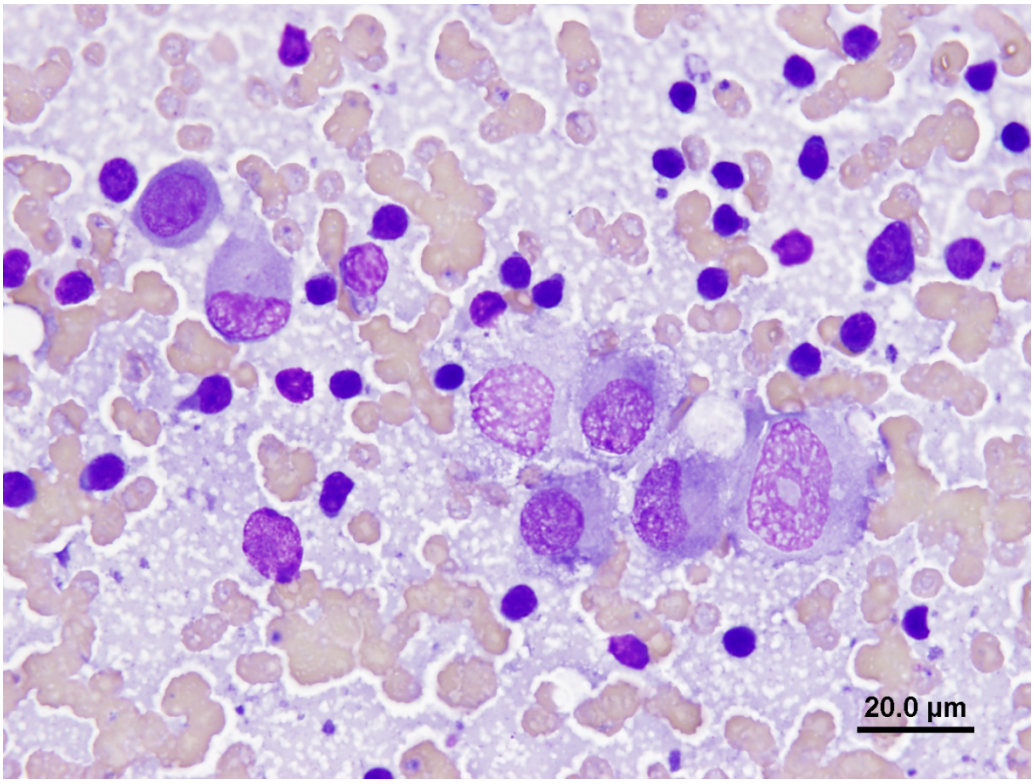


Figure 3
Fine needle aspirate from a mediastinal lymph node.  Modified Romanowsky stain, 100x.

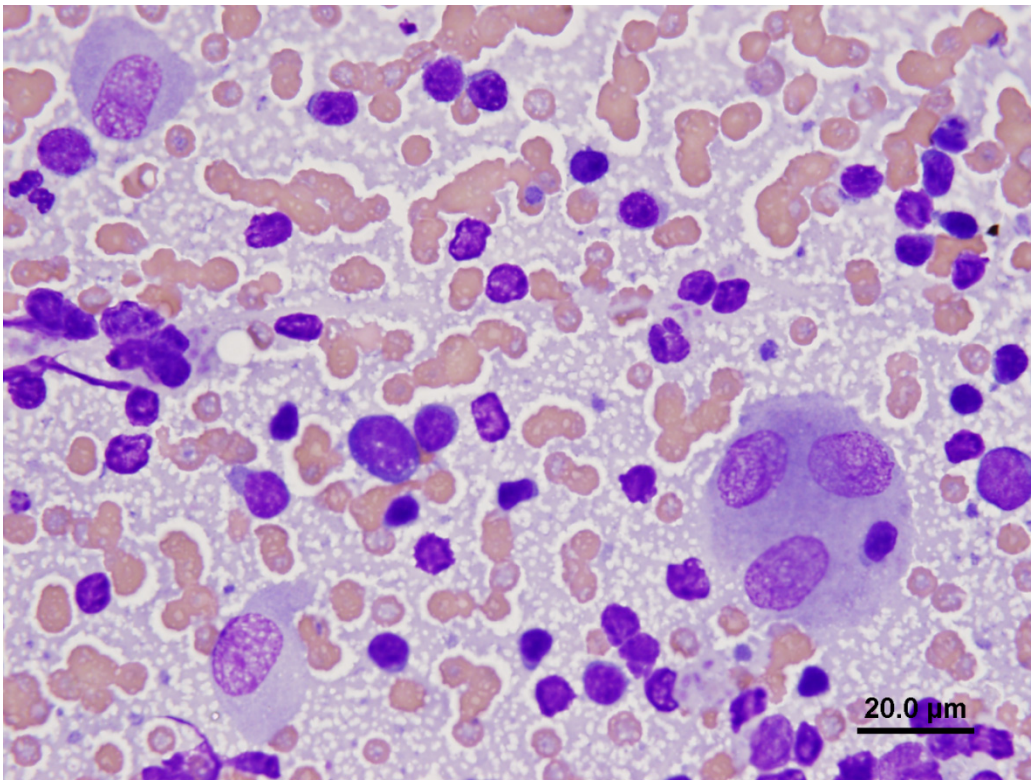

Figure 4
Fine needle aspirate of mediastinal lymph node. Modified Romanowsky stain, 100x.

**Questions**:
What are the differential diagnoses based on the cytology, signalment, history, and clinical signs?
What further tests could be done to reach a definitive diagnosis?

**Further investigations and discussion:**

**Cytology of abdominal mass:**

The specimen has moderate cellularity and is composed of a monomorphic cell population exfoliating individually and in loose aggregates in a moderately bloody background. The cells are large (20-50 microns in diameter), are round to spindloid in shape, and have indistinct cell borders. The N:C ratio is variable but generally 1:1. Cells have moderate to abundant, basophilic cytoplasm that contains low numbers of clear vacuoles, and an eccentrically located, oval to lobulated nucleus with finely to coarsely stippled chromatin. There is mild to moderate anisokaryosis and anisocytosis, and occasional multinucleated cells are noted.

**Cytology of mesenteric lymph node:**

Cells similar to the ones observed in the mesenteric mass are scattered among a heterogeneous population of lymphocytes. Occasionally these large cells exhibit erythrophagocytosis, and rare mitotic figures are noted.

**Cytologic diagnosis:**

Possible mesenchymal neoplasia (differential diagnosis histiocytic sarcoma or poorly differentiated sarcoma) with lymph node involvement, or severe granulomatous inflammation

**Additional Findings:**
A laparotomy was performed and a 4x5 cm mass associated with the pyloric region of the stomach and portion of the duodenum was removed. Histologically, a large mass composed of several pyogranulomas circumscribed by fibrous tissue markedly expanded the tunica muscularis and serosa of the stomach and duodenum, and extended to the pancreas. The centers of the granulomas was composed of macrophages, variable numbers of degenerate and non-degenerate neutrophils, and rare lymphocytes, with occasional necrotic = debris. The pyogranulomas were surrounded by a band of lymphocytes and plasma cells and thick bands of connective tissue. The granulomas multifocally extend into and expand the submucosa. Immunohistochemical staining for coronavirus was applied to one section of the mass, and low numbers of macrophages in multiple pyogranulomas, exhibited intense cytoplasmic staining. Gram, modified acid-fast, and Gomori-Grocott methenamine silver stains were all negative.

**Histologic diagnosis:**
Severe, chronic, multifocal to coalescing, pyogranulomatous gastritis and duodenitis, with intralesional coronavirus (ferret FIP-like syndrome)

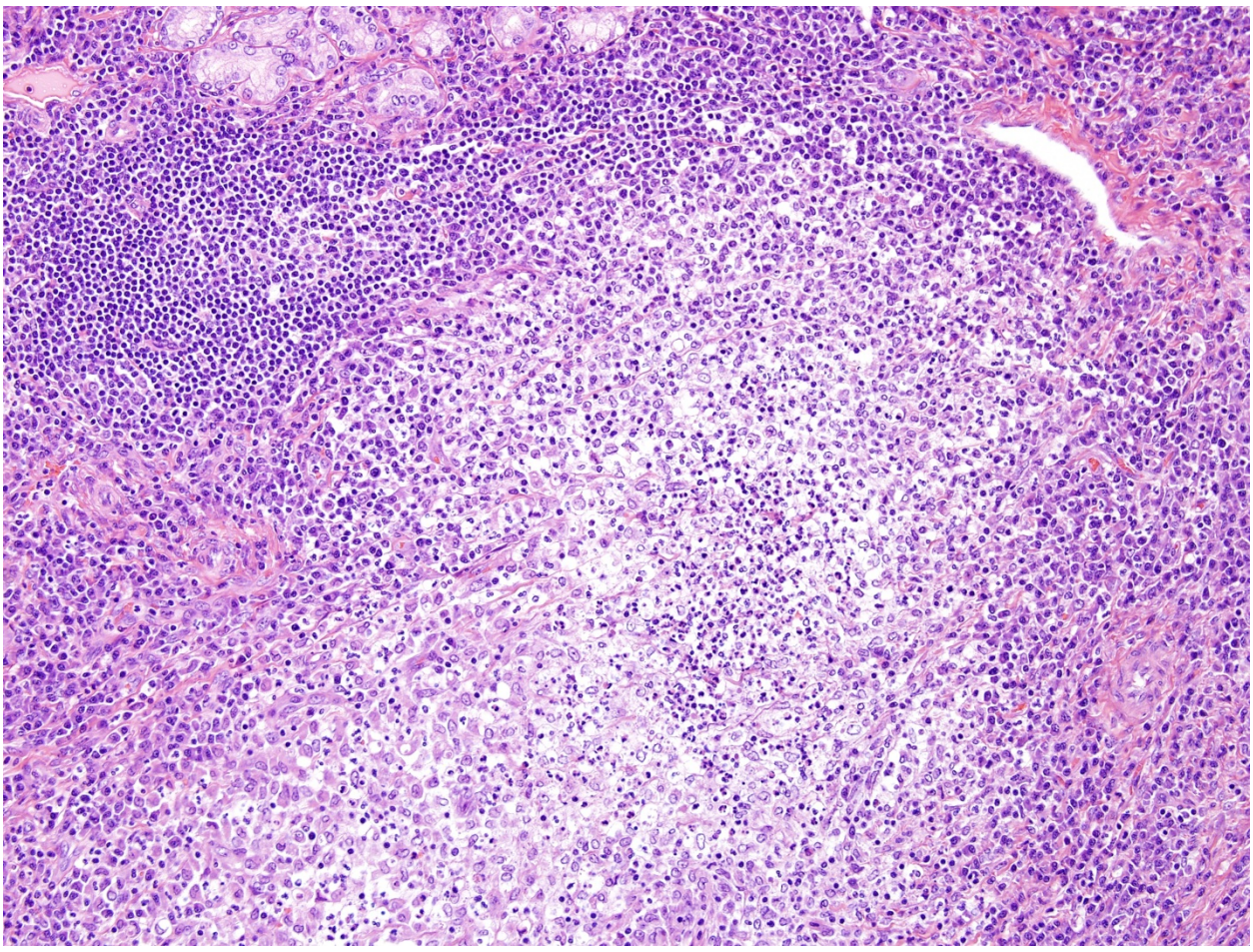

Figure 5
Histologic section of the mesenteric mass. Note the severe pyogranulomatous inflammation, with macrophages and neutrophils in the center surrounded by lymphocytes and plasma cells. H&E stain, 20x.

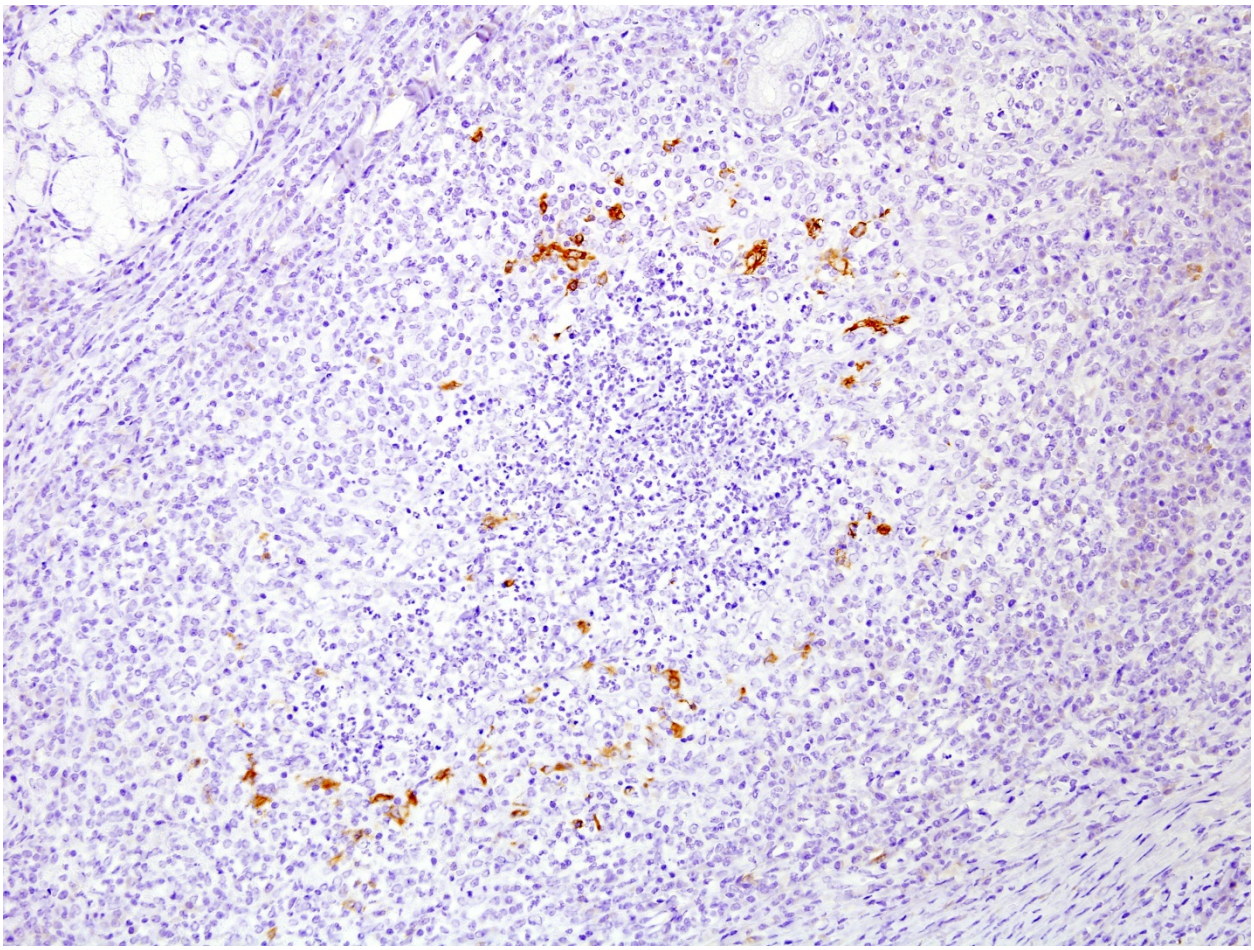

Figure 6
Histologic section of the mesenteric mass. Immunohistochemical staining for coronavirus reveals low numbers of macrophages in a granuloma exhibiting intense cytoplasmic staining. 20x.

**Case outcome:**
Due to poor prognosis, surgical complications, and progressive health decline, the owner opted for humane euthanasia.

**Discussion**:
First identified in Spain in 2006, ferret systemic coronavirus infection (FRSCV) is an emerging disease that has been recognized in pet ferrets in the USA and Europe [1, 2]. Common clinical signs include weight loss, lethargy, anorexia, vomiting, loss of body condition, ataxia, paraparesis, seizures, and head tilt [2, 4]. Less commonly, FRSCV can cause sneezing, coughing, nasal discharge, dehydration, bruxism, systolic heart murmur, jaundice, and green urine [2, 4]. Other concurrent findings of FRSCV include anemia, hyperproteinemia due to hyperglobulinemia, and leukocytosis with marked neutrophilia [2].
Much like the dry form of feline infectious peritonitis (FIP) in cats, FRSCV primarily effects juvenile and young adult ferrets with an average age on onset of 11 months [2, 4]. Another similarity between FRSCV and FIP includes a high mortality rate and short duration of illness, with an average of 69 days for FRSCV [2]. Gross pathology associated with FRSCV includes granulomatous lesions throughout the abdominal cavity, such as masses and nodules on the spleen, liver, kidneys, mesentery, and lymph nodes with concurrent organomegaly and mesenteric lymphadenopathy [2]. Histologic examination reveals severe pyogranulomatous inflammation centering on vessels, similar to dry FIP in cats [2]. Specific diagnostic

tests for FRSCV include immunohistochemistry for coronavirus, PCR for the coronavirus spike protein, and electron microscopy showing cytoplasmic viral inclusion bodies within macrophages [2, 5]. Differential diagnoses for the intestinal masses include lymphoma, mycobacteriosis nocardiosis, adrenal neoplasia, and other causes of chronic inflammation [2].

The pathogenesis of FRSCV is still largely unknown. However, phylogenetic analysis of isolated strains show the virus is more similar to ferret enteric coronavirus (FRECV) than other Group 1 coronaviruses [5]. Genetic analysis of the coronavirus spike protein indicates that FRSCV is significantly different from FRECV, and thus, a different pathotype [4, 5]. It cannot be determined based on the available data whether FRSCV evolved from *in vivo* mutations from FRECV or if both strains are circulating independently of one another [5]. Given the many similarities between FIPV and FRSCV, the viral mutations required for macrophage tropism may also be similar. The ability to infect macrophages of FIPV strains potentially has arisen from mutations in the S, 3 abc, 7a, and 7b genes compared to FCoV sequences [5]. Notably, analyzed strains of FRSCV also had mutations in spike protein and 3c-like protein genes compared to the FRECV sequence, which may mediate viral tropism to macrophages [5]. Further analysis of FRSCV and FRECV strains are required to elucidate the pathogenesis and pathophysiology of FRSCV infections.

The pleomorphism of the large cells identified in the mesenteric mass and lymph node fine needle aspirates of this case made it difficult to determine if the cells were a part of a neoplastic population or were reactive macrophages. Definitive diagnosis was achieved by histopathology and immunohistochemical staining confirming coronavirus in the cytoplasm of macrophages composing the granulomas within the abdominal cavity. The findings of this case emphasize that FRSCV should be considered as a differential diagnosis in ferrets with evidence for an abdominal mass.


1. Martínez, J., et al., *Detection of feline infectious peritonitis virus-like antigen in ferrets.* Vet Rec, 2006. **158**(15): p. 523.
2. Garner, M.M., et al., *Clinicopathologic features of a systemic coronavirus-associated disease resembling feline infectious peritonitis in the domestic ferret (Mustela putorius).* Vet Pathol, 2008. **45**(2): p. 236-46.
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4. Murray, J., M. Kiupel, and R.K. Maes, *Ferret coronavirus-associated diseases.* Vet Clin North Am Exot Anim Pract, 2010. **13**(3): p. 543-60.
5. Wise, A.G., et al., *Comparative sequence analysis of the distal one-third of the genomes of a systemic and an enteric ferret coronavirus.* Virus Res, 2010. **149**(1): p. 42-50.